

MRI of prostate cancer: Diagnosis, staging and treatment of prostate cancer

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Introduction

The clinical problems:

Prostate cancer is the most common non-cutaneous cancer and the second most common cause of cancer death in American men. The American cancer society estimates that in 2003, 220,900 new cases for prostate cancer will have been identified [1]. With the increase in the number of older people in the US (the baby-boomers), it is estimated that 450,000 new cases will be diagnosed in 2015 the US [2]. The lifetime risk of disease is 16.6% for Caucasian and 18.1% for African-Americans and a lifetime risk of death of 3.5% and 4.3% respectively. The age-adjusted mortality rose an estimated 39% from 1985 to 1997. Combined with an aging population, these factors have made prostate cancer a major medical and socioeconomic problem.

Prostate cancer remains the key disease for which this imaging is used. The incidence of prostate cancer is high with approx 230,000 men to be diagnosed in the US this year. With the aging of the baby boomers, that number is estimated to increase to over 450,000 by the year 2015. The other important fact about prostate cancer is that only approx 4-8% of men with the disease, will actually die of it. It is often thought to be a "normal" cancer of aging, as it is estimated that 80% of men who are 80 years of age will have it.

The management of men with clinically localized prostate cancer is one of the most debated and controversial topics in all of clinical medicine today. Basically there are 4 treatment choices surgery (radical prostatectomy), Radiation therapy- either external beam or brachytherapy and observation of "watchful-waiting". Some would correctly argue that the latter is actually not a therapy but is included here as imaging may play a large role in this group. Traditionally imaging has not been used much by surgeons, due to its perceived lack of sensitivity and more importantly specificity for detecting extra-glandular disease. This approach is currently undergoing a relative sea change and with good reason. Despite major advances in screening, increased PSA measurements, detection of cancer and development of nomograms for staging

between 22% and 50% of patients thought to have organ-confined disease have extra-glandular disease at pathology [3],[4, 5]

MR imaging for diagnosis and staging of prostate cancer has been clinically available and used by several centers for many years. In its history it has undergone several improvements and phases of high and low clinical impact. The history of Prostate MRI will be reviewed and the current state of the art will be presented during this lecture. Specifically this lecture will focus on the role in diagnosis, staging and treatment of prostate cancer. The newer role of MR in guiding biopsy and treatment of prostate cancer will be reviewed and examples of MR guided prostate biopsies and MR guided brachytherapy will be provided. As in many other forms of cancer, imaging is playing an ever-expanding role in tumor monitoring. Finally I will provide a brief overview of the other imaging modalities for prostate cancer, namely Ultrasound, CT and PET imaging.

MRI of the prostate

MR imaging of the prostate has been available since the late 1980's, initially using the body coil and then in the 1990's with an endorectal coil. Early work by Hricak, Schnall and others established the fundamentals of prostate MRI. They defined the appearance of the gland on standard pulse sequences, described the typical appearance of the 2 most common diseases of the prostate, namely Cancer and Benign prostatic hyperplasia. Examples will be shown. Several large multi-center trials have been performed to evaluate Prostate MRI in general and Prostate MR spectroscopy (MRSI) specifically. The original one was the Radiology Diagnostic oncology group (RDOG) trial in the late 1980's and early 1990's. This trial focused on the accuracy of MRI for staging prostate cancer in men with clinically localized disease and who had radical prostatectomy. The more recent American college of Radiology imaging network trial evaluated a very similar cohort of patients for a very different reason. In the latter ACRIN trial of MRSI the goal is to determine the accuracy of MRSI in cancer detection, within the gland, in men with known prostate cancer. The results of this trial are not available at this time but the MRSI methodology and study design will be reviewed in this lecture. A second trial of MRSI is underway in Europe and elsewhere, known as the IMAPS trial. Initial results of this trial were presented at the RSNA 2005 (Scheenen TWJ et al RSNA 2005, SSKO7-06,p 419).

Current MR imaging techniques

The current techniques require multi-planar imaging, with high spatial resolution and good contrast to noise. While this is most commonly done at 1.5T with an inflatable endorectal coil, there is a significant shift occurring towards 3T systems. For this talk the protocols and the majority of the images shown will be from 1.5T systems. The initial apparent advantages of 3T will be illustrated.

The aims of prostate MR imaging are basically two-fold

- 1) To characterize focal abnormalities and all tissues within the gland and detect cancer. This requires detailed parenchymal tissue evaluation.
- 2) To provide loco-regional staging information. This requires less detail within the prostate itself and more of the surrounding structures, lymph nodes and bones.

Thus depending on the aims of the study one of two protocols can be used. Before describing specific protocols, there are several basic issues to review. All prostate MR studies require the exam to provide excellent visualization of the prostate gland, its borders, the adjacent structures and pelvic nodes and bones[6]. The prostate is located deep in the male pelvis, just below the urinary bladder and anterior to the rectum. The bladder is drained by the urethra and this passes through the prostate to be joined by the ejaculatory ducts, at the verumontanum, in the mid-prostate. The distal urethra continues down to exit the prostate at the external urethral sphincter and pass through the uro-genital diaphragm, to become the penile urethra. A fatty layer of adventitia, which contains nerves, arteries and veins, surrounds the gland. The critical extra-glandular structures are the neurovascular bundles (NVB) and the seminal vesicles[7, 8].

Prostate MRI protocol (attention cancer detection)

Conventional T1-spin echo and T2-weighted fast spin echo scans are performed in the oblique axial plane, sagittal and/or coronal plane to obtain images throughout the prostate with nominal voxel volumes of 0.002 ml. The axial T1 and T2W images must patch slice for slice for exact correlation. These are usually obtained with 3mm slice thickness, either interleaved or with a 0.5mm gap. These are supplemented with detailed tissue imaging sequences such as T2 maps, Diffusion MRI, dynamic contrast enhanced imaging [9] [10] and Spectroscopy [11]. A 17 minute 3D spectroscopic imaging sequence with the General Electric supplied PROSE sequence (TR/TE = 1000/130 ms/ms) was performed to obtain the metabolite ratio (Cho + Cr)/Cit from nominal voxel volumes of 0.5 ml ([12] For diffusion imaging, we currently use the line scan approach pioneered by Maier [13]

Prostate MRI protocol (Staging examination)

In this protocol the attention is to the gland, tumor and surrounding tissues. Typical sequences include the basic T1 and T2W images with the endorectal coil and external arrays. This is now beginning to be supplemented by MRIS sequences in selected patients. This set of data is used to carefully evaluate the prostate capsule, NVBs and Seminal vesicles. The previous results from the RDOG trail up to the present time indicate that this can be a very accurate examination, which requires experienced radiologists interpretation [14, 15]. [16] [17, 18]

Then the lymph nodes and bones are evaluated with axial imaging to the level of the kidneys. This can be done with or without contrast agents. New methods of nodal imaging include MR lymphangiography [19], [20] which uses the small iron oxide particle agents or Combidex. This agent appears very useful in detecting micro-metastases in side normal sized lymph nodes, thus allowing us to take nodal detection to another level. However it is not yet in widespread use in the US, though many centers elsewhere are using it with good results [10].

MR guided prostate biopsy

MR guided prostate biopsy has been introduced as a means to attempt to solve the difficulty some patients have in achieving a diagnosis [21]. We have shown its value in several clinical conditions [22], the two major groups being men with a rising PSA, despite repeated negative biopsies in the past, or men who have had rectal surgery and do not have access for Transrectal Ultrasound guided biopsy. In our program men have the pre-biopsy imaging performed as described above in the first protocol. This allows us to use these images to define targets for biopsy. The importance of multi-parametric examination of the images will be discussed and techniques used in our center for image registration and real-time display during MR guided biopsies will be illustrated. The results of our first 53 patients were presented at ISMRM 2005 and are under review at this time. We showed that the procedure was feasible, safe and led to increased detection of cancer in the MRI defined targets. This approach is now under investigation by several other centers.

MR guided cancer treatment

MR guided interventions in prostate cancer image-guided therapy and diagnosis can be guided by different image modalities with transrectal ultrasound (TRUS) being the most widely used method. Ultrasound provides good delineation of the prostate margin, simplicity of imaging, relatively low cost compared to other modalities, and availability. Ultrasound is used for guidance of both prostate biopsies and brachytherapy. An additional advantage is its ability to detect in real time the movements of the prostate gland introduced by performing the treatment, which in turn allows for adjustments of therapy delivery. Fusion of intra-operative ultrasound images with pre-treatment endorectal MRI (erMRI) images provides great improvement in visualization of anatomical structures[23]. CT-guidance was used primarily for prostate biopsies but has also been introduced in prostate cancer therapy guidance[24]. CT provides clear visualization of prostate boundaries with high spatial resolution and contrast among different organs. Additional placement of a Foley catheter in the bladder allows for good visualization of the urethra that is helpful in avoiding urethral damage during treatment delivery.

MR guided brachytherapy is performed in an open magnet-GE Signa SP at 0.5T. It allows the operator access to the prostate through the perineum and allows placement of the needles, pre-loaded with I-125 seeds to be performed. This is possible, as MRI provides superior visualization of the prostate and its zonal anatomy, as well as depiction of surrounding vital organs like the rectum, neurovascular bundles, and urethra. It also provides good visualization of the tumor location within the prostate gland. The development of open MRI made it possible to perform prostate brachytherapy and biopsy under MR guidance [25].

MRI is also being used in different ways to monitor the effect of new drugs on prostate cancer. Recent results show its potential role as a surrogate marker, combined with PSA to track the drug effect prior to other treatments [26]

Summary

The role of MRI in prostate cancer is wide and diverse with many different applications, both new and established. No doubt there will be more presented at this meeting, attesting to the fact this is an exciting time for prostate imaging and MRI will continue to play a major role in assisting patients and their doctors both detect and manage prostate cancer.

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